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Dated: 9/16/05

Signature: *Jeanne M. Brashear*
(Jeanne M. Brashear)

Docket No.: 19036/40139
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Akinori Hatanoto

Application No.: 10/520,037

Confirmation No.: 9381

Filed: June 30, 2005

Art Unit: 1614

For: Skin Preparation for External Use

Examiner: Zohreh Vakili

DECLARATION UNDER 37 C.F.R. § 1.132 OF MS. ATSUKO OGAWA

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Ms. Atsuko Ogawa, hereby state as follows:

1. I am familiar with the subject matter disclosed and claimed in the above-referenced patent application (hereinafter, "the patent application"). I currently hold the position of Chief Staff at Noevir Co.Ltd. and have been engaged in the research of cosmetics for the past twenty-three years.

2. The patent application is directed in part to external preparations (i.e., compositions) comprising polyethylene glycol (PEG) having a degree of polymerization of 2,000 to 50,000 (or polyvinyl alcohol) and glycolic acid, wherein the external preparation has a pH of 2.0 or less. Such compositions are useful methods requiring the chemical peeling of skin. Exemplary claims defining the invention are appended hereto as Exhibit A.

3. The purpose of this declaration is to summarize experiments performed after the filing date of the application which confirm the advantageous results of the external preparations (i.e., compositions) recited in the claims. The experiments described herein demonstrate that compositions comprising PEG within the claimed range and having a pH of

2.0 or less is more effective than a composition comprising the same PEG and having a pH greater than 2.0.

4. The following describes work performed by me and those working with me in my laboratory.

5. *Preparation of test compositions:* Composition B was prepared as described in Example 1 described in Table 1 of the application (see page 7 of the application). Composition B comprises polyethylene glycol (PEG) having a degree of polymerization of 45,000 and a pH of about 1.4. Compositions A, B and D, were prepared as described above for Composition B, except that Composition A comprises polyethylene glycol (PEG) having a degree of polymerization of 7,000; Composition C comprises PEG having a degree of polymerization of 2,000 and Composition D comprises a PEG having a degree of polymerization of 400. Composition E comprises PEG having a degree of polymerization of 45,000 and a pH of about 3.5.

6. *Evaluation of Application Performance and Effectiveness of the Tested Compositions:* Seven 5 cm² inflamed areas were defined on the forearms of ten male subjects between the ages of twenty and forty. Compositions A-E were applied to the inflamed areas with a flat brush. Application performance of the various compositions was evaluated and classified into one of two groups ("the composition was capable of being applied in a uniform manner" or "the composition, when applied, was liable to be uneven").

After ten minutes the test compositions were washed away with water. After twenty-four hours, the forearms of the subjects were visually examined and the effectiveness of each composition was determined by examining the stratum corneum (i.e., the top layer of skin) for uniform peeling. The effectiveness of each composition was classified into one of three groups ("after application of the composition, the stratum corneum was uniformly peeled," "after application of the composition, the stratum corneum was peeled patchwise" and "after application of the composition, the stratum corneum was not peeled"). Results indicated that the compositions comprising PEG having a degree of polymerization between 2,000 and 50,000 (i.e., Compositions A-C) were more effective than the compositions comprising PEG having a degree of polymerization below 2,000 (i.e., Composition D). See Table A below.

A comparative example between Compounds B and E is set forth in Table B below. Table B shows that the composition comprising PEG within the claimed range at a pH of 3.5 (i.e., Composition E) had good application performance (i.e., was capable of being applied in a uniform manner), but did not demonstrate the same peeling effectiveness (stratum corneum was not peeled in most panels) as the Composition B (i.e., composition comprising PEG within the claimed range at a pH of 1.4). Thus, the data present herein also demonstrates that a composition comprising a pH of 2.0 or less is required for the most effective results.

Table A.

	Degree of Polymerization	Viscosity on the next day	Application Performance		Effectiveness		
			Capable of being applied in a uniform manner	Liable to be uneven	Stratum corneum was uniformly peeled	Stratum corneum was peeled patchwise	Stratum corneum was not peeled
Composition A	7,000	80	9	1	7	3	0
Composition B	45,000	100	9	1	8	2	0
Composition C	2,000	72	9	1	8	2	0
Composition D	400	Unable to evaluate (water-like)	2	8	2	8	0

Table B

	Composition B	Composition E
Purified Water	45	41
70% by weight aqueous solution of glycolic acid	30	30
2% by weight aqueous solution of PEG with polymerization degree of 45,000	25	25
Sodium Hydroxide	-	4
Total (% by weight)	100	100
pH	1.4	3.5

	Composition B	Composition E
Application performance	Uniform	Uniform
Effectiveness	Favorable (stratum corneum was uniformly peeled)	No effect (stratum corneum was <u>not</u> uniformly peeled)

7. *Evaluation of the Stability of the Tested Compositions:* The viscosity of Compositions B and E on the next day was assumed to be 100. The viscosities of compositions A, C, and D on the next day are shown in Table A in a relative value.

8. I hereby confirm that the experiments discussed in Sections 4-7 of this declaration are an accurate description of experiments in which I have participated with others in my laboratory, and the results that we obtained.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the above-referenced patent application and any patent issued therefrom.

Date: Sep. 16 / 2008

By: 小川 篤子
Ms. Atsuko Ogawa

Exhibit A

1. (Previously presented) An external preparation for skin which comprises glycolic acid and polyethylene glycol having a polymerization degree of from 2000 to 50000, wherein the preparation has a pH of 2.0 or less.
- 2-4. (Canceled)
5. (Previously presented) The external preparation for skin according to claim 1 wherein the preparation has a pH of 1.4 or less.
6. (Previously presented) An external preparation for skin which comprises glycolic acid and polyvinyl alcohol, wherein the preparation has a pH of 2.0 or less.
7. (Previously presented) The external preparation of claim 6, wherein the preparation has a pH of 1.4 or less.
8. (Previously presented) A method of chemically peeling skin comprising contacting the skin with the preparation of claim 1.
9. (Previously presented) A method of chemically peeling skin comprising contacting the skin with the preparation of claim 5.
10. (Previously presented) A method of chemically peeling skin comprising contacting the skin with the preparation of claim 6.
11. (Previously presented) A method of chemically peeling skin comprising contacting the skin with the preparation of claim 7.
12. (New) The external preparation of claim 1, wherein the polyethylene glycol has a polymerization degree of about 45,000.